GENE EXPRESSION

Corrected: Publisher Correction

Sequence meets space

A new computational method integrates RNA single-cell sequencing and spatial data.

Spatial transcriptomics and single-cell sequencing are the two vanguard approaches for studies of heterogeneity in gene expression. A handful of methods have recently been used in attempts to map cells in space via projection of the rich transcriptomic information from single-cell sequencing onto spatial coordinates determined by in situ hybridization. Guo-Cheng Yuan of the Dana-Farber Cancer Institute, Long Cai of the California Institute of Technology and their colleagues now integrate these data to ask a different question: what aspects of a cell's state are driven by position, and what aspects are intrinsic?

The researchers focused on the mouse visual cortex, for which both single-cell RNA-seq (scRNA-seq) and sequential fluorescence in situ hybridization (seqFISH) data exist. In a 1-mm^2 section of tissue, they were able to quantify the expression of 125 genes in nearly 1,600 cells from seqFISH data. The use of a machine learning classifier on fewer than 50 genes from scRNA-seq data allowed them to distinguish major cell types, and application of this subset to the seqFISH results gave good cell-type classification.

After mapping cell types, the researchers developed a hidden Markov random field model to carve the cortex into spatial domains. The approach uses a graph representation of cells' spatial relationships to search for neighbors with shared expression. Gene expression may fall into a domain because cells within that domain are of the same type (cell-intrinsic) or because the same genes across cell types respond similarly to environmental cues (cell-extrinsic). This analysis identified nine domains in the mouse visual cortex, including some that reflect its layered anatomical structure.

Glutamatergic cells were scattered across all nine domains, and astrocytes were detected in five domains, which suggests that these cells can occupy different cell states. The researchers also cleverly used domain genes to identify spatial structure across single-cell transcriptomes, highlighting how the integration of imaging and sequencing data enables the transfer of complementary information.

Tal Nawy

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Research papers
Zhu, Q. et al. Identification of spatially associated subpopulations by combining scrNAseq and sequential fluorescence in situ hybridization data. *Nat. Biotechnol.* https://doi.org/10.1038/nbt.4260 (2018).

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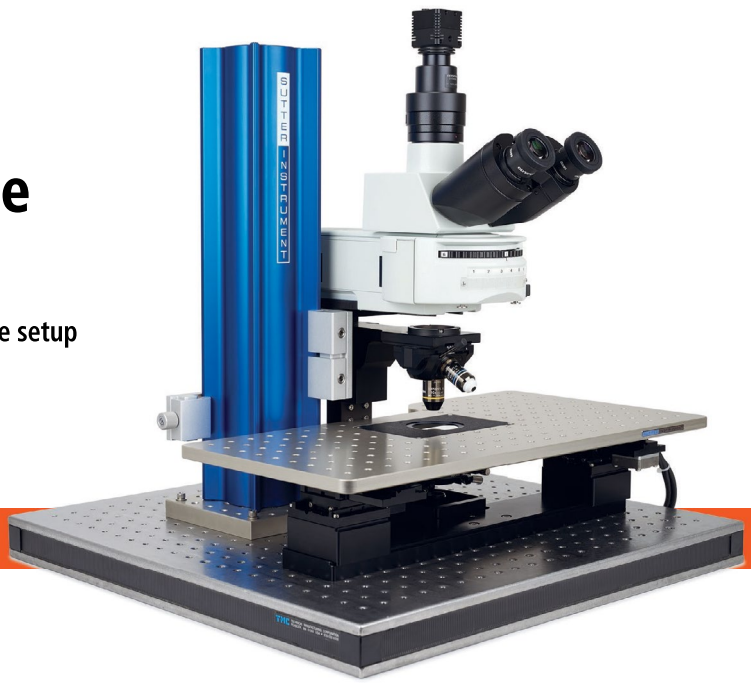

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